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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,757	01/03/2007	Emma Kvitnitsky	KVITNITSKY=1A	5965
1444 7590 07/12/2010 BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303				
EXAMINER CHANDRAKUMAR, NIZAL S				
ART UNIT 1625		PAPER NUMBER		
MAIL DATE 07/12/2010		DELIVERY MODE PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/553,757

Applicant(s)

KVITNITSKY ET AL.

Examiner

NIZAL S. CHANDRAKUMAR

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/28/2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7-15 and 19-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-15 and 19-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S508)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicants response filed 06/28/2010 is acknowledged.

Claims 1-5, 7-15, 19-31 are in the case.

Claims 1-5, 7-15, 19-31 were examined to the extent that they read on the elected group of compounds.

The elected group is limited to compounds of the formula (I) wherein R3 and R4 are hydrogens.

The finality of the previously office action is withdrawn.

Response to applicants Remarks:

Claim Rejections - 35 USC § 112

Upon further consideration, previously presented rejection under 35 USC § 112 is withdrawn.

New Rejection:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the

subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

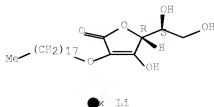
Claims 1-5, 7-15, 19-31 rejected under 35 U.S.C. 103(a) as being unpatentable over Shimizu et al. (EP 0619313 A1), (reference provided by the applicant).

Shimizu et al., teach page 2 lines 29 to page 3, line 9, page 6 line 24 to page 7 line 3 and Example 1, compounds of the instant formula wherein R2 is lithium.

On page 6, the preparation of the compounds is disclosed.

In the above process, the compound (I) can be prepared by reacting ascorbic acid or isoscorbic acid with a protecting agent such as methoxymethyl chloride, ethoxymethyl chloride, benzyl bromide, trimethylsilyl chloride, dimethyl-tert-butylsilyl chloride or the like according to per se known methods to obtain 3-O-ether, followed by reaction of the resulting 3-O-ether with a compound of the formula: R¹-Z wherein R¹ is as defined above and Z is halogen (e.g., chlorine, bromine, etc.). This reaction is carried out in the presence of an inorganic acid. Examples of the inorganic acid include alkaline metal hydroxides (e.g., sodium hydroxide, potassium hydroxide, etc.), alkaline metal salts (e.g., sodium carbonate, potassium carbonate, etc.) and the like. This reaction is carried out in a solvent which does not hinder the reaction. Examples of the solvent include amides (e.g., dimethylformamide, hexamethylphosphoramide, etc.), sulfoxides (e.g., dimethyl sulfoxide, etc.), cyclic ethers (e.g., tetrahydrofuran, etc.) and the like. These solvents can be used alone or in combination of the two or more of them. The reaction temperature is about 1 to 18 hours. The reaction temperature is about 10 to 60 °C.

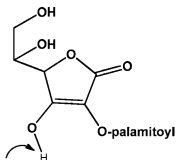
The lithium salt of 2-O-alkylascorbic acids of the present invention shows free-radical scavenging and anticancer actions in experiments in vitro using lipid peroxidation enzyme, phospholipid hydrolyase A₂ and The preparation of a lithium salt



is exemplified on page 9, Example 1 which discloses that by reacting lithium carbonate with substituted ascorbic acid, lithium salt can be made. Shimizu et al., also disclose biological property corresponding to instant claims 15, 19-31 limitations.

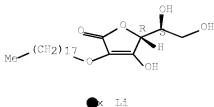
While Shimizu et al exemplifies lithium salt; the instant base claim does not include lithium salts but includes other salts such as sodium or potassium salts.

It would have been to one of skilled in the art that replacing lithium carbonate with other metal bases such as sodium carbonate or sodium hydroxide would provide corresponding sodium salt. This is because, in the above-mentioned substituted ascorbic acid exemplified by



the hydrogen shown by the arrow is acidic and would react with any (metal) bases to make the corresponding (metal) salts. Thus the instant compounds are salts of many known ascorbic acid compounds except lithium salts. Different salts of the same acid are suggestive of one another and no secondary teaching is needed.

Replacement of Li metal in the following Shimizu et al disclosure



with other metal is obvious:

One of ordinary skill in the art would be motivated to make alternate salt forms prior art compounds by replacing lithium ion with other cations because it is well known in the art that the therapeutic and cosmetic properties (drug effects) of the compounds of ascorbic acid derivatives depend on the ascorbic acid portion of the formulae. Further it is well known that different cations allow for routine optimization of physical and chemical properties such as solubility, stability etc. known active ingredients. As such the instantly claimed compounds would have been suggested as alternate forms of commercially important ascorbic acid derivatives.

Claims 1-5, 7-15, 19-31 rejected under 35 U.S.C. 103(a) as being unpatentable over Strelchler et al. (US 6143906) further in view of Shimizu et al. (EP 0619313 A1).

Strelchler et al. teach in claim 1 (column 11) ascorbic acid derivatives corresponding to compounds of the instant formula I wherein R3 and R4 of the instant case corresponds to R1 and R2 of prior art; R2 of the instant case corresponds to R3 of prior art; R1 of the instant case corresponds to C6 acyl group of the prior art. Strelchler et al.

discloses the synthesis of four ascorbic acid derivatives, in particular, (i) 2,5,6-O-trisorbyl-L-ascorbic acid; (ii) 5,6-O-isopropylidene-2-O-sorbyl-L-ascorbic acid; (iii) 2-O-sorbyl-L-ascorbic acid; and (iv) 6-O-palmitoyl-2-O-sorbyl-L-ascorbic acid, asserting that these derivatives are more stable than ascorbic acid.

(see affidavit filed 8/31/2010, page 16-17).

Strechler et al. do not teach all possibilities of the R1 variable. Strechler et al.s compounds are limited to 2-sorbyl, that is C6-acyl derivatives, while the instant compounds are C8-C18 acyl derivatives. Strechler et al. do not teach R1-alkyl (that is 2-alkoxy) compounds of the instant formula I; Shimizu et al., teach lithium salts of alkoxy compounds.

The instantly claimed compounds correspond to salts of well known alkyl and acyl derivatives of ascorbic acid. Making salts of known acids is using different bases is within the skill of a laboratory technician. As discussed above, Shimizu et al., teach how to make lithium salt using a lithium base, namely lithium carbonate. Thus it is within the knowledge of a technician that sodium carbonate would make sodium salt; or amine base would make ammonium salt. One of ordinary skill in the art would be motivated to make alternate salt forms prior art compounds by replacing lithium ion with other cations because it is well known in the art that the therapeutic and cosmetic properties (drug effects) of the compounds of ascorbic acid derivatives depend on the ascorbic acid portion of the formulae and the knowledge that the different cations allow for optimization of physical and chemical properties such as solubility, stability etc. As such the instantly claimed compounds would have been suggested as alternate forms of commercially important ascorbic acid derivatives. A compound and its properties are

inseparable. Obviousness based on similarity of structure and functions entails motivation to make the claimed compound in expectation that compounds similar in structure will have similar properties; therefore, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new compounds. A strong case of prima facie obviousness has been established.

Claim Rejections - 35 USC § 102

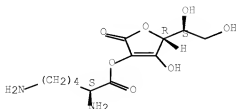
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, is rejected under 35 U.S.C. 102(b) as being anticipated by Roomi et al. US 6864284.

Roomi et al. teach CAS RN# 500903-97-9



corresponding to compound of the instant elected formula wherein

R1 is amino acid group,

R2 is ammonium.

Note that the above structure is zwitterionic, ascorbic acid portion being acidic and lysine being basic forming the (internal) ammonium salt

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 7-15, 19-31 rejected under 35 U.S.C. 103(a) as being unpatentable over Shimizu et al. (EP 0619313 A1) and Roomi et al. US 6864284 independently and collectively.

Shimizu et al. teach lithium salt of the instantly claimed acids (vide infra).

Roomi et al. teach ammonium salt of the instantly claimed acids (vide infra).

Shimizu et al. and Roomi et al. teach metal salt as well as ammonium salt ascorbic acids. The difference is that these prior art references do not teach all the conceivable combination of the instantly claimed variables. Different salt of the same

acids (for example glycine salt as in claim 9 for lysine salt or Na salt for Li salt) are suggestive of one another. Making salts of known acids is using different metal bases within the skill of a laboratory technician. As discussed above, Shimizu et al., teach how to make lithium salt using lithium base (lithium carbonate). One of ordinary skill in the art would be motivated to make alternate salt forms prior art compounds by replacing lithium ion with other cations because it is well known in the art that the therapeutic and cosmetic properties (drug effects) of the compounds of ascorbic acid derivatives depend on the ascorbic acid portion of the formulae and the knowledge that the different cations allow for optimization of physical and chemical properties such as solubility, stability etc. As such the instantly claimed compounds would have been suggested as alternate forms of commercially important ascorbic acid derivatives. A compound and its properties are inseparable. Obviousness based on similarity of structure and functions entails motivation to make the claimed compound in expectation that compounds similar in structure will have similar properties; therefore, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new compounds. A strong case of prima facie obviousness has been established.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nizal S Chandrakumar/

Examiner, Art Unit 1625

/Janet L. Andres/

Supervisory Patent Examiner, Art Unit 1625